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Tissue factor coagulation pathway and blood cells activation state in renal insufficiency.

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INTRODUCTION: Atherosclerotic cardiovascular disease is the le cause of the increased morbidity and mortality observed in uremic patients. Thrombosis is an important contributor to the evolution o atherosclerotic lesions. The physiologically-relevant blood clotting depends on binding of activated factor VII (FVIIa) to exposed tissu factor (TF) on activated/damaged cells. MATERIALS AND METHODS: A cross-sectional study was performed on three age-sex-matched groups of individuals: one group of 50 patients on maintenance hemodialysis (D group), one of 50 patients with a non-dialysed renal insufficiency (ND group) and one of 50 healthy controls (HC group). We studied basal plasma concentrations of F factor VII-related antigen (FVIIAg), soluble TF, tissue factor pathw inhibitor (TFPI), TF-dependent circulating monocytes procoagular activity (TF-dMPA), tissue factor-dependent plasma reactivity to activated protein C (TF-aPC), D-dimers (D-Di), and circulating ma of cellular activation/injury: soluble thrombomodulin (sTM), circu microparticles (microP), soluble leukocyte, endothelial and platele selectins (sL-selectin, sE-selectin, sP-selectin), soluble intercellula adhesion molecule 1 and vascular cell adhesion molecule 1 (sICAM and sVCAM-1). Their variations induced, in hemodialysis patients dialysis run were thereafter studied RESULTS: Values of FVIIa, FVIIa/FVIIAg ratio, sTF, TFPI, TF-dMPA, D-Di, sTM, microP, sL and sP selectins, sICAM-1 and sVCAM-1 increased all along the hierarchy HC group/ND group/D group. Microparticles were main platelet origin, to a lesser extent of monocyte origin. Dialysis indu

increase of FVIIa, sTF, TF-dMPA and circulating markers of cellu activation/injury. Strong correlations were observed between FVIIa/FVIIAg ratio and serum creatinine levels, sTF, TF-dMPA, s sE-selectin, sVCAM-1. The TF-aPC was impaired in the ND and t group, and the lower values were, in the D group, associated with antecedents of vascular access thrombosis. CONCLUSION: Renal insufficiency is associated to an activation of the tissue factor coagulation pathway, to a platelet, monocyte and endothelial activation/injury and to a deficient tissue-factor induced response t activated protein C which culminate in end-stage disease and are increased by hemodialysis runs. This contributes to linked coagula and cellular conditions for an enhanced atherosclerosis progressio to the TF pathway activation, the therapeutic use of recombinant T should be evaluated.

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In vivo competition between a metallothionein regulat element and the SV40 enhancer.

Scholer H, Haslinger A, Heguy A, Holtgreve H, Karin M.

The human metallothionein-IIA (hMT-IIA) gene contains an enha element within its 5' regulatory region. This enhancer element can compete with the SV40 enhancer for one or more cellular factors i vivo. The competition between the two elements is modulated by cadmium, an inducer of hMT-IIA transcription. The data presentec consistent with a model in which heavy metal ions control the abil the hMT-IIA enhancer to bind a positive factor, leading to increase transcription. The same factor is required for maximal activity of t SV40 enhancer, which suggests that viruses utilize factors that hav normal role in cellular gene expression to control their own genes.

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